



COPY OF PAPERS
ORIGINALLY FILED

SEQUENCE LISTING

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<110> Buelow, Roland
Platzer, Josef
van Schooten, Wim
Buelow, Jens-Ulrich

<120> PRODUCTION OF HUMANIZED ANTIBODIES IN TRANSGENIC
ANIMALS

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<140> 09/921,819

<141> 2001-08-03

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<170> PatentIn Ver. 2.1

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<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

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<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence:primer

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<212> DNA

<213> cow

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

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<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence:primer

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<210> 12
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 <212> DNA
 <213> rabbit

<220>
 <221> Unsure
 <222> (997)
 <223> n at position 997 is uncertain

<220>
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<210> 13

<211> 668

<212> DNA

<213> rabbit

<400> 13

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<210> 14

<211> 45

<212> PRT

<213> camel

<400> 14

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Leu Ser Val Cys Tyr Ser Ala Thr Val Thr Leu Phe Lys
35 40 45

<210> 15

<211> 44

<212> PRT

<213> Homo sapiens

<400> 15

Glu Leu Gln Leu Glu Glu Ser Cys Ala Glu Ala Gln Asp Gly Glu Leu
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Thr Leu Phe Leu Leu
20 25 30

Ser Val Cys Tyr Ser Ala Thr Val Thr Phe Phe Lys
35 40

<210> 16

<211> 44

<212> PRT

<213> Homo sapiens

<400> 16

Glu Leu Gln Leu Glu Glu Ser Cys Ala Glu Ala Gln Asp Gly Glu Leu
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Leu Ile Thr Leu Phe Leu Leu
20 25 30

Ser Val Cys Tyr Ser Ala Thr Val Thr Phe Phe Lys
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<210> 17

<211> 44

<212> PRT

<213> Homo sapiens

<400> 17

Glu Leu Gln Leu Glu Glu Ser Cys Ala Glu Ala Gln Asp Gly Glu Leu
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Thr Leu Phe Leu Leu
20 25 30

Ser Val Cys Tyr Ser Ala Thr Val Thr Phe Phe Lys
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<210> 18
<211> 44
<212> PRT
<213> mouse

<400> 18
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu Leu
20 25 30

Ser Val Cys Tyr Ser Ala Ala Val Thr Leu Phe Lys
35 40

<210> 19
<211> 44
<212> PRT
<213> mouse

<400> 19
Gly Leu Asp Leu Asp Asp Val Cys Ala Glu Ala Gln Asp Gly Glu Leu
1 5 10 15

Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu Leu
20 25 30

Ser Val Cys Tyr Ser Ala Ser Val Thr Leu Phe Lys
35 40

<210> 20
<211> 45
<212> PRT
<213> mouse

<400> 20
Pro Gly Leu Gln Leu Asp Glu Thr Cys Ala Glu Ala Gln Asp Gly Glu
1 5 10 15

Leu Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu
20 25 30

Leu Ser Val Cys Tyr Ser Ala Ala Val Thr Leu Phe Lys
 35 40 45

<210> 21
 <211> 44
 <212> PRT
 <213> mouse

<400> 21
 Glu Leu Glu Leu Asn Glu Thr Cys Ala Glu Ala Gln Asp Gly Glu Leu
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu Leu
 20 25 30

Ser Val Cys Tyr Ser Ala Ser Val Thr Leu Phe Lys
 35 40

<210> 22
 <211> 44
 <212> PRT
 <213> mouse

<400> 22
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Asp Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu Leu
 20 25 30

Ser Val Cys Tyr Ser Ala Ser Val Thr Leu Phe Lys
 35 40

<210> 23
 <211> 44
 <212> PRT
 <213> sheep

<400> 23
 Leu Leu Leu Glu Glu Glu Ser Cys Ala Asp Ala Gln Asp Gly Glu Leu
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Asp Gly Leu Trp Thr Thr Ile Ser Ile Phe Ile Thr Pro Phe Leu Leu
 20 25 30

Ser Val Cys Tyr Ser Ala Thr Val Thr Leu Phe Lys
 35 40

<210> 24
<211> 44
<212> PRT
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<400> 24
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Ser Val Cys Tyr Ser Ala Thr Val Thr Leu Phe Lys
35 40

<210> 25
<211> 19
<212> PRT
<213> cow

<400> 25
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Asp Gly Leu

<210> 26
<211> 19
<212> PRT
<213> cow

<400> 26
Leu Leu Leu Glu Glu Glu Ile Cys Ala Asp Ala Gln Asp Gly Glu Leu
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Asp Gly Leu

<210> 27
<211> 43
<212> PRT
<213> rabbit

<400> 27
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Gly Leu Trp Thr Thr Ile Thr Ile Phe Ile Ser Leu Phe Leu Leu Ser
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Val Cys Tyr Ser Ala Thr Val Thr Leu Phe Lys
35 40

<210> 28
<211> 27
<212> PRT
<213> camel

<400> 28
Val Lys Trp Ile Phe Ser Ser Val Val Glu Leu Lys Arg Thr Ile Val
1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ser
20 25

<210> 29
<211> 27
<212> PRT
<213> Homo sapiens

<400> 29
Val Lys Trp Ile Phe Ser Ser Val Val Asp Leu Lys Gln Thr Ile Ile
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Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 30
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<400> 30
Val Lys Trp Ile Phe Ser Ser Val Val Asp Leu Lys Gln Thr Ile Ile
1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 31
<211> 27
<212> PRT
<213> Homo sapiens

<400> 31

Val Lys Trp Ile Phe Ser Ser Val Val Asp Leu Lys Gln Thr Ile Ile
1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 32
<211> 27
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<213> mouse

<400> 32
Val Lys Trp Ile Phe Ser Ser Val Val Glu Leu Lys Gln Thr Leu Val
1 5 10 15

Pro Glu Tyr Lys Asn Met Ile Gly Gln Ala Pro
20 25

<210> 33
<211> 27
<212> PRT
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<400> 33
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1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 34
<211> 27
<212> PRT
<213> mouse

<400> 34
Val Lys Trp Ile Phe Ser Ser Val Val Glu Leu Lys Gln Thr Leu Val
1 5 10 15

Pro Glu Tyr Lys Asn Met Ile Gly Gln Ala Pro
20 25

<210> 35
<211> 27
<212> PRT
<213> mouse

<400> 35

Val Lys Trp Ile Phe Ser Ser Val Val Gln Val Lys Gln Thr Ala Ile
1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 36
<211> 27
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<400> 36
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1 5 10 15

Pro Asp Tyr Arg Asn Met Ile Gly Gln Gly Ala
20 25

<210> 37
<211> 27
<212> PRT
<213> rabbit

<400> 37
Val Lys Trp Ile Phe Ser Ser Val Val Glu Leu Lys His Thr Ile Ala
1 5 10 15

Pro Asp Tyr Arg Asn Met Met Gly Gln Gly Ala
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<210> 38
<211> 8
<212> PRT
<213> sheep

<400> 38
Val Lys Trp Ile Phe Ser Ser Val
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<210> 39
<211> 29
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<220>
<223> Description of Artificial Sequence:primer

<400> 39

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29

<210> 40

<211> 28

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 40

gtcgacgccc ctcgatgcac tcccagag

28

<210> 41

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 41

ggtaccctct ccctccccca cgccgcagc

29

<210> 42

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 42

atatctcaga actggctgtc cctgctgtag tacacgg

37

<210> 43

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 43

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27

<210> 44

<211> 28
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 <220>
 <223> Description of Artificial Sequence:primer

 <400> 44
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<210> 45
 <211> 38
 <212> DNA
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 <220>
 <223> Description of Artificial Sequence:primer

 <400> 45
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<210> 46
 <211> 36
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Description of Artificial Sequence:primer

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<210> 47
 <211> 35
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Description of Artificial Sequence:primer

 <400> 47
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<210> 48
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 48

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<210> 49

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 49

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42

<210> 50

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 50

ctaggtacca gcaggtgggg gcacttctcc c

31

<210> 51

<211> 1719

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:human

immunoglobulin heavy chain C γ 1 gene segment
flanked by nucleotides derived from the rabbit
heavy chain.

<400> 51

tgacctacct accctgccaa ggtcaggggt cctccaaggc aagggatcac atggcaccac 60
ctctcttgca gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag 120
cacctctggg ggcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt 180
gacggtgtcg tggaaactcag gcgccctgac cagcggcggt cacaccttcc cggtgttctt 240
acagtcttca ggactctact ccctcagcag cgtgggtgacc gtgccctcca gcagcttggt 300
caccagacc tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa 360
agttggtgag aggccagcac agggaggagg ggtgtctgtt ggaagccagg ctcagcgctc 420
ctgcctggac gcatcccggc tatgcagccc cagtccaggg cagcaaggca ggccccgtct 480

```

gcctcttcac ccggaggcct ctgcccgcct cactcatgct cagggagagg gtcttctggc 540
tttttcccca ggctctgggc aggcacaggc taggtgcccc taaccaggc cctgcacaca 600
aaggggcagg tgctgggctc agacctgcca agagccatat ccgggaggac cctgcccctg 660
acctaagccc accccaaagg ccaaactctc cactccctca gctcggacac cttctctcct 720
cccagattcc agtaactccc aatcttctct ctgcagagcc caaatcttgt gacaaaactc 780
acacatgccc accgtgcccc ggtaagccag cccaggcctc gccctccagc tcaaggcggg 840
acaggtgccc tagagtagcc tgcattccag gacaggcccc agccgggtgc tgacacgtcc 900
acctccatct cttcctcagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc 960
ccaaaaccca aggacaccct catgatctcc cggaccctct aggtcacatg cgtgggtggg 1020
gacgtgagcc acgaagaccc tgaggtcaag ttcaactggg acgtggacgg cgtggagggt 1080
cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtggtcagc 1140
gtcctcaccg tcttgacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 1200
aacaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg tgggaccctg 1260
ggggtgctgag ggccacatgg acagaggccg gctcggccca ccctctgccc tgagagtgc 1320
cgctgtacca acctctgtcc ctacagggca gccccgagaa ccacaggtgt acaccctgc 1380
cccattcccgg gatgagctga ccaagaacca ggtagcctg acctgcctgg tcaaaggctt 1440
ctatcccagc gacatcgccg tggagtggga gagcaatggg cagccggaga acaactacaa 1500
gaccacgct cccgtgctgg actccgacgg ctcttctctc ctctacagca agctcaccgt 1560
ggacaagagc aggtggcagc aggggaacgt cttctcatgc tccgtgatgc atgaggctct 1620
gcacaaccac tacacgcaga agagcctctc cctgtctccg ggtaaatgag cgctgtgccc 1680
gcgagctgcc cctctccctc cccccacgc cgcagctgt 1719

```

<210> 52
 <211> 390
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: a VH gene
 segment encoding a human VH element polypeptide
 sequence, with flanking sequences derived from
 rabbit immunoglobulin DNA sequences.

```

<400> 52
tgagtgcagc tgtcctgacc atgtcgtctg tgtttgcagg tgtccagtgt gaggtgcagc 60
tggtggagtc cgggggaggc ctgctccagc caggggggac cctgagactc acctgcgcag 120
tctctggatt caccctcagt agctatgcaa tgagctgggt ccgccaggct ccagggaagg 180
ggctggaatg ggtagcagcc attagtggta gtggtagcac atactacgcg gacagcgtga 240
aaggccgatt caccatctcc agagacaact ccaagaacac gctgtatctg caaatgaaca 300
gtctgagagc cgaggacacg gccgcctatt actgtgcgaa agacacagtg agggggccctc 360
aggctgagcc cagacacaaa cctccctgca 390

```

<210> 53
 <211> 445
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: containing a

human immunoglobulin light chain Ck gene segment
flanked by 50 nucleotides derived from the rabbit
light chain immunoglobulin Kappal gene.

```
<400> 53
catccacatg gcacccaggg gagatgtcca ctggtaccta agcctcgcca tcctgtttgc 60
ttctttcctc aggaactgtg gctgcacat ctgtcttcat cttcccgcca tctgatgagc 120
agttgaaatc tggaactgcc tctgttgtgt gcctgctgaa taacttctat cccagagagg 180
ccaaagtaca gtggaagggtg gataacgccc tccaatcggg taactcccag gagagtgtca 240
cagagcagga cagcaaggac agcacctaca gcctcagcag caccctgacg ctgagcaaag 300
cagactacga gaaacacaaa gtctacgcct gcgaagtcac ccatcagggc ctgagctcgc 360
ccgtcacaaa gagcttcaac aggggagagt gttagagcga gacgcctgcc agggcacccg 420
cagcgaccct gaggcccagc ctcgc                                     445
```

```
<210> 54
<211> 632
<212> DNA
<213> Artificial Sequence
```

```
<220>
<223> Description of Artificial Sequence:a Vk gene
segment encoding a human Vkelement polypeptide
sequence, flanking by sequences derived from
rabbit immunoglobulin DNA.
```

```
<400> 54
ggcaggctgc tcccacccca tgcaggaggc agtaccagge aggaccagc atggacatga 60
gggtccctgc tcagtcctcg ggactcctgc tgctctggct cccaggtaag gagggaaaca 120
acaaaaattt tattcagcca gtgtagccac taatgcctgg cacttcagga aattcttctt 180
agaacattac taatcatgtg gatatgtgtt tttatgttcc taatatcaga taccagatgt 240
tacatccaga tgaccagtc tccatcctct ctgtctgcat ctgtgggaga cagagtcacc 300
atcacttgcc gagccagtc gggcattagc aattacttag cctggtatca gcagaaacca 360
gggaagggtc ccaagctcct gatttatgct gcacccactt tgcaatctgg ggtcccatcg 420
cgtttcagtg gcagtggatc tgggacagat ttcactctta ccatcagcag cctgcagcct 480
gaagatgttg ccacctatta ctgtcaaaaag tacaacagtg cccctccact tttcggcgga 540
gggaccaagg tggagatcaa acgtaagtgc actttcctaa tgttcctcac cgtttctgcc 600
tgatttgttt gctttttcca ttttttcgct at                                     632
```

```
<210> 55
<211> 70
<212> DNA
<213> Artificial Sequence
```

```
<220>
<223> Description of Artificial Sequence:primer
```

```
<400> 55
catacacagc catacatagc cgtgtggccg ctctgcctct ctcttgagg tatggacagc 60
aagcgaaccg                                     70
```

<210> 56
<211> 71
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:primer

<400> 56
atcagggtga cccctacgtt acactcctgt caccaaggag tgggagggac tcagaagaac 60
tcgtcaagaa g 71

<210> 57
<211> 419
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:a gene encoding
human immunoglobulin light chain constant region
Clambda2 flanked by nucleotides derived from the
chicken light chain gene.

<400> 57
catacacagc catacatagc cgtgtggccg ctctgcctct ctcttgcagg tcagcccaag 60
gctgccccct ccgtcactct gttcccgcgc tcctctgagg agcttcaagc caacaaggcc 120
acactgggtgt gtctcataag tgacttctac ccgggagccg tgacagtggc ttggaaagca 180
gatagcagcc ccgtcaaggc gggagtggag accaccacac cctccaaaca aagcaacaac 240
aagtacgcgg ccagcagcta tctgagcctg acgcctgagc agtggaagtc ccacagaagc 300
tacagctgcc aggtcacgca tgaagggagc accgtggaga agacagtggc ccctacagaa 360
tgttcatagt agtcccactg gggatgcaat gtgaggacag tggttcctca ccctccctg 419

<210> 58
<211> 416
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:a VJ gene
segment encoding a human VJ immunoglobulin
polypeptide, with flanking sequences derived from
chicken immunoglobulin DNA.

<400> 58
ttgccgtttt ctcccctctc tcctctccct ctccaggttc cctgggtgcag tcagtgtctga 60
ctcagccgcc ctcggtgtca gcagccccgg gacaagaagt cacgatctcc tgctccgggt 120
ctagtagcaa cattggcgat aatttcgtct cttggtacca gcagctgcct ggcactgccc 180
ctaagcttct gatctatgat aacaacaaga gaccctcggg catccctgac cgattctccg 240

gttccaaatc eggcacctca gccacattag gcatcactgg gctccaaacc ggcgacgagg 300
ctgactatta ctgtgggact tgggacagca gcctttctgt tggatatgtt gggggcggga 360
cacgcgtgac cgtcctaggt gagtcgctga cctcgtctcg gtctttcttc ccccat 416